PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference HP1344	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/FI2005/000037	International filing date *(day/month/year)* 19-01-2005	Priority date *(day/month/year)* 23-02-2004
International Patent Classification (IPC) or national classification and IPC See Supplemental Box		
Applicant HORMOS MEDICAL LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13-10-2005	23-05-2006
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Per Renström/MP Telephone No. +46 8 782 25 00

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Cover sheet

International patent classification (IPC)

A61K9/14 (2006.01)
A61K31/085 (2006.01)
A61K 9/20 (2006.01)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI2005/000037

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____ ,
which is the language of a translation furnished for the purposes of:

- ☐ international search (Rules 12.3(a) and 23.1(b))
- ☐ publication of the international application (Rule 12.4(a))
- ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) -- see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-23	YES
	Claims	-	NO
Inventive step (IS)	Claims	-	YES
	Claims	1-23	NO
Industrial applicability (IA)	Claims	1-23	YES
	Claims	-	NO

2. Citations and explanations (Rule 70.7)

The following documents are considered relevant:

A: Remington: The Science and Practice of Pharmacy, 20th Ed. chapter 45; Oral Solid Dosage Forms, pages 865-871 (granulation methods).
B: US6245352 B1
C: US6525084 B2

In document A, different granulation methods are presented. Wet granulation is called "the most widely used and most general method of tablet preparation". See page 865.

Document B discloses a pharmaceutical formulation which comprises tamoxifen citrate in a tablet. The tablet is manufactured by mixing the intra-granular components using a solvent such as water. The resultant granules are then dried and mixed with inter-granular components, and the resultant mixture is pressed into a tablet mould. See column 3 line 55 - column 4 line 4.

Document C pertains to a granulate prepared by a wet granulation method. Active substances mentioned include a variety of selective estrogen receptor modulators (SERM), e.g. toremifene, droloxifene and 4-hydroxytamoxifene. See the abstract and claim 5.

The present application relates to a method for the granulation of ospemifene, a SERM. The method involves wet granulation of the active substance together with intra-granular excipients such as binders, disintegrants and/or diluents.

.../...

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of: Box V

The difference between documents A-C listed above and the present application is that the present application presents ospemifene as an active agent. The problem posed in the application is that of manufacturing granules and tablets containing ospemifene. However, from all documents A-C, it is obvious that wet granulation is a well known method of manufacturing granules and tablets containing active substances.

Thus, a person skilled in the art who is posed with a problem of manufacturing a pharmaceutical composition containing an active substance such as ospemifene, would consider the possibility of wet granulation. The use of excipients such as binders, disintegrants and diluents is also well known in the art.

Claim 11 of the present application relates to dry granulation. It is to be noted that the applicant has not shown this method. However, dry granulation is also a well known method of manufacturing pharmaceutical compositions (see e.g. document A).

Thus, all claims 1-23 lack the requirement of inventive step. The view that the advantage of granulate formulation is surprisingly high for ospemifene, as put forth in the letter of 2005-10-13, is not considered to change this situation.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
Öhman, Ann-Marie
Kaivokatu 15 B 23
FI-20520 Turku
Finland

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* 25 -05- 2005

Applicant's or agent's file reference
HP1344

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/F I2005/000037	19.01.2005	23.02.2004

International Patent Classification (IPC) or both national classification and IPC
A61K 31/085, A61K 9/16, A61K 9/20

Applicant
Hormos Medical Corporation et al

1. This opinion contains indications relating to the following items:

- [x] Box No. I Basis of the opinion
- [ ] Box No. II Priority
- [ ] Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV Lack of unity of invention
- [x] Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI Certain documents cited
- [ ] Box No. VII Certain defects in the international application
- [ ] Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further opinions, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/SE
Patent- och registreringsverket
Box 5055
S-102 42 STOCKHOLM

Facsimile No. +46 8 667 72 88

Authorized officer
Ingrid Eklund/Els

Telephone No. +46 8 782 25 00

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/F I2005/000037

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language, _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/F I2005/000037

Box No. V **Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-23	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-23	NO
Industrial applicability (IA)	Claims	1-23	YES
	Claims		NO

2. Citations and explanations:

The following documents are considered relevant:

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The present application relates to a method for the granulation of ospemifene, a SERM. The method involves wet

.../...

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of: Box V

granulation of the active substance together with intra-granular excipients such as binders, disintegrants and/or diluents.

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Thus, all claims 1-23 lack the requirement of inventive step.